

Manifestações Cutâneas da COVID-19: Uma Série de Casos do Brasil

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RESUMO – Introdução: O Brasil apresenta dados alarmantes e crescentes sobre infecção e óbitos por SARS-CoV-2. Existem mais de 4 500 000 de casos confirmados e mais de 137 000 mortes, ocupando o segundo lugar no ranking mundial de pessoas infectadas. Além do acometimento dos sistemas respiratório, cardiovascular, renal e neurológico, esse vírus também causa lesões cutâneas inespecíficas nos pacientes. Pouco se sabe sobre a fisiopatologia do envolvimento cutâneo. No momento, não podemos prever uma diferença de prognóstico com base nas lesões cutâneas. **Métodos:** Conduzimos um estudo de casos observacional de 25 pacientes afetados pela SARS-CoV-2 que apresentavam lesões dermatológicas. Descrevemos as características clínicas e epidemiológicas de cada caso, demonstrando o polimorfismo das lesões cutâneas e também fazendo uma correlação com a cronologia dos sintomas sistêmicos apresentados. **Resultados:** Vinte e cinco casos de COVID-19 com manifestações cutâneas (urticária, erupção cutânea eritematosa, erupção maculopapular, prurido, lesões do tipo eritema multiforme, eczema disidrótico, lesões eritematosas acrais) foram observados durante, após e antes dos sintomas sistêmicos. Alguns casos com envolvimento cutâneo também foram observados como sintomas isolados de infecção viral. Esses dados demonstram o polimorfismo clínico relacionado ao envolvimento cutâneo dos pacientes infectados pela SARS-CoV-2, enfatizando a importância da suspeita clínica pelo dermatologista no tratamento dos casos suspeitos no cenário epidemiológico atual. **Conclusão:** Embora o número de casos no cenário mundial pareça estar regredindo, a infecção pelo SARS-CoV-2 fará parte do dia a dia do dermatologista. Enquanto não tivermos uma vacina amplamente disponível e a pandemia assumir um perfil endêmico, precisamos estar atentos a essas manifestações, não apenas para o diagnóstico adequado, indicação de isolamento do paciente, como também todos os procedimentos de biossegurança necessários em clínicas de dermatologia.

PALAVRAS-CHAVE – Brasil; COVID-19; Infecções por Coronavírus; Manifestações Cutâneas; SARS-CoV-2.

Cutaneous Manifestations of COVID-19: A Case Series from Brazil

ABSTRACT – Introduction: Brazil has presented alarming and growing data on infection and deaths from SARS-CoV-2. There are more than 4 500 000 confirmed cases and more than 137 000 deaths ranking second in the world ranking of infected people. In addition to the involvement of the respiratory, cardiovascular, renal and neurological systems, this virus also causes non-specific skin lesions in same patients. Little is known about the pathophysiology of cutaneous involvement. At this moment, we cannot predict a difference in prognosis based on skin lesions. **Methods:** We conducted an observational case study of 25 patients affected by SARS-CoV-2 who had dermatological lesions. We described the clinical and epidemiological characteristics of each case, demonstrating the polymorphism of the skin lesions and also making a correlation with the chronology of presented systemic symptoms. **Results:** Twenty five cases of COVID-19 with cutaneous manifestations (urticaria, erythematous rash, maculopapular eruption, pruritus, erythema multiforme-like lesions, dyshidrotic eczema) were observed during, after and before systemic symptoms. A few cases with skin involvement were also observed as isolated symptoms of the viral infection. These data demonstrate the clinical polymorphism related to skin involvement of patients infected with SARS-CoV-2, emphasizing the importance of clinical suspicion by dermatologists when handling suspected cases in the current epidemiological scenario. **Conclusion:** Although the

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number of cases in the world stage seems to be regressing, infection by SARS-CoV-2 will be part of the dermatologist's daily routine. As long as we do not have a widely available vaccine and the pandemic takes on an endemic profile, we need to be aware of these manifestations, not only for the proper diagnosis, indication of patient isolation, as well as all the necessary biosafety procedures in dermatology clinics.

KEYWORDS – Brazil; Coronavirus Infections; COVID-19; SARS-CoV-2; Skin Manifestations.

INTRODUCTION

Coronavirus are encapsulated RNA viruses belonging to the *Coronaviridae* family and to the order *Nidovirales*, widely distributed among humans and other mammals.¹

In 2019, a series of pneumonia cases of undetermined cause with clinical involvement similar to viral pneumonias appeared in China.² Sequenced analyzes of the patients' lower respiratory tract identified a new version of the virus, the new coronavirus 2019 (nCoV-19).¹⁻³

The disease became known as "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) and gained global proportions, configuring a pandemic, given its high transmission capacity between humans. Patients infected with SARS-CoV-2 may be oligosymptomatic or even asymptomatic, but a large part of those affected develop symptoms such as fever, cough, anosmia, dysgeusia, myalgia and headache, in addition to lung disease, which can cause respiratory failure and respiratory syndrome acute severe (SRAG), which generates the need for hospitalization and intensive care.^{1,3,4} Besides involvement of the digestive, cardiovascular and nervous system, this virus also generates nonspecific changes in the skin, and as far as we know they are not fully related to prognosis.⁵⁻¹¹

COVID-19 pandemic fatalities are rare before puberty (<10 years of age), and the vulnerability of males to severe disease has been constantly reported over the past months of pandemic.⁶

Brazil currently has more than 4,5 million confirmed cases and almost 137 thousand deaths, occupying the second place in the world in number of cases, behind only the United States.⁷

In this article we will present a series of 19 cases of Brazilian patients infected with SARS-CoV-2 and who developed dermatological lesions. We will describe the polymorphism of the skin lesions and make a correlation in relation to the chronology of the infection, aiming at whether the dermatological lesions occurred before, during, after or not related to the systemic symptoms due to this infection. We hope to contribute to a better understanding of dermatological involvement and to warn about the possibility of the occurrence of dermatological lesions, as a prodromal sign or unique symptom of COVID-19.

MATERIAL AND METHODS

An observational study was carried out of patients seen at outpatient dermatology consultations and of patients hospitalized for clinical management in Rio de Janeiro state, Brazil. We evaluated 25 cases of patients affected by

SARS-CoV-2 who had dermatological lesions. We analyzed objectively their data such as sex, age, comorbidities, laboratory tests related to SARS-CoV-2 infection, contact with confirmed cases, type of dermatological lesions, their topography, chronology according to systemic symptoms and which systemic symptoms were presented.

RESULTS

We analyzed data from 25 patients, aged between 14 and 92 years old. Of this population, 9 patients did not have comorbidities, 3 were overweight, 4 had systemic arterial hypertension, one of whom was also affected by hypothyroidism, another by chronic obstructive pulmonary disease (COPD) and another one by autoimmune mediastinitis; 1 dementia, 1 depression, 1 obesity, 1 asthma, 1 obesity and asthma, 2 dyslipidemia and 1 autoimmune disease.

Among all patients, 23 had positive reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2, one had positive IgM serology and another one had positive IgG serology. They presented skin lesions of the following types: urticaria / annular urticarial rash (Fig. 1), pruritic erythematous rash (Fig. 2), erythema multiforme like rash



Figure 1 - Annular urticarial rash on the dorsa of the forearms (Patient N° 3).



Figure 2 - Pruritic erythematous rash on the foot (Patient N° 14).



Figure 4 - Pruritic erythematous papulovesicular rash that preceded the onset of flu-like symptoms (Patient N° 15).

(Fig. 3), pruritic erythematous papulovesicular rash (Fig. 4), livedo reticularis (Fig. 5), dyshidrosiform papulovesicular rash (Fig. 6), cyanosis and acral erythematous lesions.

Three patients did not present any systemic symptoms,

sixteen had skin lesions after the symptoms, three during the symptoms and three had skin lesions preceding the systemic symptoms. Patients number 11 and 20 died due to COVID-19 infection. Details are in Table 1.



Figure 3 - Erythema multiforme-like rash on the palms (Patient N° 18).



Figure 5 - Livedo reticularis on the breast (Patient N° 12).

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Figure 6 - Dyshidrosiform papulovesicular rash on the dorsal aspect of the hands (Patient N° 6).

DISCUSSION

Brazil has presented alarming and growing data on infection and deaths from SARS-CoV-2. There are more than 4 500 000 confirmed cases and more than 137 000 deaths ranking second in the world ranking of infected people.¹⁰

In Lecco, Italy, an observational study was conducted with a sample of patients infected with SARS-CoV-2. From the collected data (88 patients), 18 patients (20.4%) developed cutaneous manifestations. Eight patients developed cutaneous involvement at the onset, 10 patients after the hospitalization.⁸

Skin involvement was observed in 0.2%-1.2% in 1099 patients with laboratory-confirmed COVID-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through January 2020.⁹

According to the Brazilian Ministry of Health, Rio de Janeiro has an alarming number of confirmed cases, with a total of 277 439 infected.¹⁰ However we did not find any records of the frequency of cutaneous involvement in infected patients.

Spanish researchers conducted a study in which data were collected from 375 patients infected with SARS-CoV-2 who had cutaneous manifestations.

Among these patients 19% presented pseudo-chilblain lesions, 9% vesicular lesions, 19% urticarial lesions, 47% maculopapular lesions and 6% livedo / necrosis lesions.¹²

The chronology of skin manifestations has also been described. Among pseudo-chilblain lesions, 7% occurred before, 34% during and 59% after systemic symptoms. Among vesicular lesions, 15% occurred before, 56% during and 29% after systemic symptoms. Of the urticaria lesions, 4% before, 61% during and 35% after symptoms. The maculopapular lesions

occurred in 5% before, 61% during and 34% after symptoms. Livedo / necrosis lesions occurred in the proportion of 5% before, 86% during and 10% after systemic symptoms.¹²

In our study we evaluated 25 patients infected with SARS-CoV-2 who had cutaneous lesions. The frequency of the types of skin lesions presented was 28% for urticarial lesions, 16% erythematous rash, 4% erythema multiforme like rash, 24% papulovesicular rash, 8% livedo reticularis, 4% dyshidrosiform papulovesicular rash, 4% cyanosis, 4% pruritus and 8% for acral erythematous lesions.

Concerning the chronology of skin involvement 12% had cutaneous lesions before the symptoms, 12% at the same time and 64% after onset of systemic symptoms, wherea 12% of patients did not present any systemic symptoms related to COVID-19.

CONCLUSION

It is of great importance that the dermatologist be aware of the chronology of cutaneous involvement of COVID-19. Few cases may present with skin lesions as an isolated symptom, while other skin signs may precede systemic involvement. This clinical perception may guarantee a more effective and safer approach, both in terms of preventing the spread of the virus, by isolating these patients with suggestive epidemiological data, as well as detailed clinical follow-up of patients, with greater vigilance regarding the development of severe symptoms.

Although the number of cases on the world stage seems to be regressing, infection by SARS-CoV-2 will be part of the dermatologist's routine. As long as we do not have a widely available vaccine and the pandemic takes on an endemic profile, we must be attentive to these manifestations, not only for the proper diagnosis, indication of patient isolation, as well as all the necessary biosafety procedures in dermatological clinics.

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Table 1 - Manifestações cutâneas da COVID-19 numa série de casos do Brasil

Nº	Gen-der	Age	Comorbidity	RT-PCR SARS-CoV-2/ Serology	Type of skin lesion	Topography	Chronology in relation to SS onset	Systemic symptoms
1	M	27	Overweight	+	Urticaria	Disseminated	Concomitant	Fever, myalgia, anosmia, cough, headache
2	F	41	None	+	Urticaria	Disseminated	After SS	Fever, myalgia, anosmia, headache
3	F	33	None	+	Urticaria	Disseminated	After SS	Fever, cough, anosmia
4	F	35	Overweight	+	Urticaria	Disseminated	After SS	Fever, myalgia, anosmia, cough, headache
5	F	27	None	+	Urticaria	Disseminated	After SS	Fever, myalgia, anosmia, cough, dyspnoea
6	F	42	None	+	Dyshidrosiform papulovesicular rash	Hands	None	None
7	M	37	SAH	+	Papulovesicular rash	Chest	After SS	Fever, dyspnoea, myalgia, cough, headache, anosmia
8	F	25	None	+	Papulovesicular rash	Facial	Concomitant	Fever, Cough
9	F	33	None	+	Papulovesicular rash	Disseminated	Before SS	Fever, cough, headache, dyspnoea
10	M	39	Depression	+	Erythematous rash	Acral	After SS	Fever, cough, dyspnoea
11	F	92	SAH/ hypothyroidism	+	Erythematous rash	Hands	After SS	Cough, dyspnoea (evolved to death)
12	F	28	Overweight	+	Livedo reticularis	Breast	After SS	Fever
13	M	75	Dementia	+	Erythematous rash + livedo reticularis	Facial / acral	After SS	Cough, dyspnoea
14	M	43	Overweight	+	Pruritic erythematous rash	Disseminated	After SS	Fever, myalgia, chest pain
15	M	74	SAH / autoimmune mediatitis	+	Pruritic erythematous Papulovesicular rash	Disseminated	Before SS	Cough, dyspnoea
16	M	44	None	+	Pruritic erythematous rash	Disseminated	After SS	Fever, cough, chest pain
17	F	44	None	+	Pruritus	Disseminated	After SS	Myalgia, cough, headache
18	F	33	Asthma/obesity	+	Erythema multi-forme like	Hands	Before SS	Respiratory failure, cough, fever
19	M	54	Dyslipidemia	IgG+	Papulovesicular rash	Zosteriform	None	None
20	M	60	SAH /COPD	IgM +	Cyanosis	Acral	After SS	Fever, cough, headache, dyspnoea (evolved to death)
21	F	54	Dyslipidemia	+	Urticaria	Trunk / arms	After SS	Fever, dyspnoea, myalgia, cough, anosmia
22	M	14	Obesity	+	Acral erythematous lesions	Legs (acral)	After SS	Fever, dyspnoea, myalgia, cough, chest pain
23	F	34	Autoimmune disease	+	Urticaria	Disseminated	Concomitant	Cough
24	M	38	Asthma	+	Acral erythematous lesions	Legs (acral)	None	None
25	F	69	None	+	Papulovesicular rash	Anterior trunk	After SS	Fever, myalgia, cough, headache

M: male; F: female; SAH: systemic arterial hypertension; +: A positive RT-PCR test for SARS-CoV-2 from a nasopharyngeal swab, unless otherwise specified; SS: systemic symptoms; COPD: chronic obstructive pulmonary disease.

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